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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/160,067 | 09/24/1998 | WALTER H. GUNZBURG | GSF98-04A | 5908 |

21005 7590 11/18/2002

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| EXAMINER | |
|---|---|
| KAUSHAL, SUMESH | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | 25 |

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/160,067 | GUNZBURG ET AL. | |
| | Examiner | Art Unit | |
| | Sumesh Kaushal Ph.D. | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for R ply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4 and 6-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4, 6-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## *DETAILED ACTION*

Applicant's response filed on 06/25/02 and 09/23/02 has been acknowledged.

*Claim 10 was amended.*
*Claims 1-4 and 6-22 were pending and were examined in this office action.*

*The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.*

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

### *Double Patenting*

Claims 1-4 and 6-22 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being un-patentable over claims 1-24 of co-pending Application No. 09/442,979, for the same reasons of record as set forth in the office action mailed on 12/21/01. The applicant will address the rejection upon an indication that there is allowable subject matter in the referenced files.

### *Claim Rejections - 35 USC § 103*

Claims 1-4, 6-9, 15-19 and 21-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over of Tai et al (FASEB Journal 7: 1061-1069, 1993) and Merten et al.

(Cytotechnology 7(2): Abstract, 1991) in view of Wei et al. (Human Gene Therapy 5: 969-978, 1994) for the same reasons of record as set forth in the office action mailed on 12/21/01.

The applicant argues that the combined teaching of Tai, Wei and Merten do not suggest to the person of ordinary skill in the art that they should encapsulate the cytochrome P450 2B1-producing fibroblast of Wei with capsules of Tai and Merten (response, page 4, para.2). The applicant argues that Tai make it clear that the gene product should be released from the capsule into the environment. The applicant argues that Wei teaches the possibility of transferring the cytochrome P450 2B gene to the neighboring tumor cells (response, page 5, para.3). The applicant argues that invention as claimed relates to a capsule wherein the membrane is permeable to prodrug molecules and cytochrome P450 and the cytochrome P450 expressed by the gene are retained within the capsule (response, page 6, para.1). The applicant further argues that prior art combination of record has been made with advantage of impermissible hindsight and thus is not proper (response, page 7, para.2). The applicant concluded that combined teaching of Tai, Wei and Merten do not render the instant invention obvious.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Tai clearly teaches that appropriate semipermeability is required that allow easy diffusion of secreted gene product without compromising the immunoisolating properties of the membrane (Tai page 1061, col.2). Tai further teaches the control of membrane permeability by adjusting sodium alignate and poly-l-lysine concentration (page 1062, fig-1; page 1063, fig-2, fig-3). Tai clearly suggested the manipulation of membrane permeability to avoid immune response. Similarly, Mertin teaches an encapsulation method which result in the retention of a secreted product while allowing the survival of encapsulated cells in a growth media. Mertin further teaches retention or release of secreted products by selecting a retention or product releasing capsule system (Mertin page 123-125, table 1-2, especially page 128, col.2, para. 3). Wei teaches genetically engineered mouse fibroblasts that produce Cytochromoe P450, wherein the P450 activates an inert prodrug like CPA into cytotoxic metabolites. Thus, it would have been obvious to one ordinary skill in the art at the time of filing to modify the teaching of Tai and Merten who in teaches the encapsulation of genetically engineered cells with selected membrane permeability, with the teaching of Wei who teaches genetically engineered cells that produces p450 which activates an inert prodrug. One would have been motivated to encapsulate

the cytochrome p450 producing cells in order to retain the P450 gene product within the capsule (Marten)) or to avoid immune rejection (Tai). One would have a reasonable expectation of success because prior art clearly teaches that manipulation of pore size of capsule membrane is well within the reach of one ordinary skill in the art (see Merten, page 128, col.2 para 3). Therefore, invention as claimed is prima facie obvious in view of cited art.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Irem

Yucel Ph.D. can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

*S. Kaushal*
**PATENT EXAMINER**

Scott D. Priebe

**SCOTT D. PRIEBE, PH.D**
**PRIMARY EXAMINER**